DURECT Announces Plans to Submit to FDA a Full Response to the POSIMIR® Complete Response Letter

Live Webcast Today at 10:30 a.m. Eastern Time

CUPERTINO, Calif., Feb. 27, 2019 /PRNewswire/ — DURECT Corporation (Nasdaq: DRRX) today announced it has completed a comprehensive review of its POSIMIR® (bupivacaine extended-release solution) program and plans to submit a full response to the Complete Response Letter (CRL) it previously received from U.S. Food and Drug Administration (FDA). The submission will request FDA approval of POSIMIR based on what the Company and its advisors believe is adequate evidence of both safety and efficacy.

DURECT commissioned the advisory services of Dr. Lee S. Simon to evaluate the adequacy of the existing POSIMIR package to address the issues raised in FDA correspondence, including the CRL. Dr. Simon is a physician and research scientist who served as the FDA's Division Director of Analgesic, Anti-inflammatory and Ophthalmologic Drug Products from 2001 to 2003. Dr. Simon is a Principal at SDG, LLC, an FDA advisory firm. Under Dr. Simon's leadership, the Company conducted a thorough review of the data and regulatory package for POSIMIR, including extensive analyses of the data from the PERSIST clinical study which the Company conducted at the FDA's request. The review of the data package was in the context of the feedback received from FDA, including the CRL and other FDA communications, in order to make a determination as to next steps for POSIMIR. Based on these analyses, the Company has decided to move forward and Dr. Simon is leading the process of preparing a submission to formally respond to the CRL. As the submission is intended to be a full response to a CRL, as opposed to a new NDA submission, the Company expects a 6-month FDA review period. The Company expects to make the submission in the first half of 2019.

"Working closely with DURECT's internal team, SDG has conducted a thorough review of the POSIMIR program. We believe that the present data package, which includes multiple adequate and well controlled trials, addresses the issues raised in theFDA's Complete Response Letter and, therefore, submission of a full response to the CRL is warranted," stated Dr. Simon.

"While the main focus of DURECT remains on our Epigenetic Regulator program and DUR-928, we also have legacy programs, like POSIMIR, that have significant potential value. We greatly appreciate Dr. Simon's guidance and expertise in thoroughly evaluating the POSIMIR program and the leadership he is providing to our team in preparing the response," saidJames E. Brown, President and CEO of DURECT. "We believe that, if approved, POSIMIR has an important role to play in addressing the need for additional long-acting, non-opioid products in the post-operative pain setting. If this strategy is successful we would seek to partner POSIMIR which would provide financial resources that could be directed toward the development of DUR-928."

About POSIMIR

POSIMIR is the Company's investigational post-operative pain relief depot product that utilizesDURECT's patented SABER® technology and is designed to deliver bupivacaine to provide up to 3 days of pain relief after surgery. POSIMIR has not been approved by the FDA for marketing in the U.S. for any indication.

About the POSIMIR Clinical Development Program

The POSIMIR clinical development program was designed to evaluate the safety and efficacy of POSIMIR for the treatment of post-surgical pain for up to 3 days.

In two completed adequate and well-controlled clinical trials, conducted in patients undergoing surgeries for inguinal hernia and subacromial decompression (shoulder), POSIMIR demonstrated a significant decrease in pain and opioid use over the 0-72 hour period following surgery as compared to placebo. DURECT believes that these completed trials support the efficacy of POSIMIR in post-operative pain and meet the requirements to be considered pivotal clinical trials.

In all, the Company has completed 16 clinical trials in the POSIMIR program, involving over 1,400 patients, over 850 of whom

received POSIMIR with the remainder in control groups. DURECT believes this is a sufficiently sized safety database. DURECT further believes that, with safety data from the PERSIST trial included, there are now sufficient data to addressFDA's issues raised in the CRL.

Market Opportunity

According to data published by the Center for Disease Control and Prevention, there are approximately 72 million ambulatory and inpatient surgical procedures performed annually in the U.S. Insufficient postoperative pain control remains a significant problem, with studies indicating that approximately 65% of patients experience moderate-to-extreme pain after surgery. The current standard of care for post-surgical pain includes a variety of opiate and non-opiate analgesics and muscle relaxants. While systemic opioids can effectively control post-surgical pain, they commonly cause side effects including drowsiness, constipation, nausea and vomiting, and cognitive impairment. Effective pain management can be compromised if patients fail to adhere to recommended dosing regimens because they are suffering from these side effects. Post-surgical pain also can be treated effectively with local anesthetics; however, their usefulness often is limited by their short duration of action.

Dial-In & Webcast Information
Wednesday, February 27 @ 10:30 am Eastern Time/7:30 am Pacific Time

Domestic:	1-800-347-6311
International:	1-323-794-2094
Conference ID:	3700258
Webcast:	http://public.viavid.com/index.php?id=133417

About DURECT Corporation

DURECT is a biopharmaceutical company actively developing therapeutics based on its Epigenetic Regulator Program and proprietary drug delivery platforms. DUR?928, a new chemical entity in Phase 2 development, is the lead candidate inDURECT's Epigenetic Regulator Program. An endogenous, orally bioavailable small molecule, DUR-928 has been shown in preclinical studies to play an important regulatory role in lipid homeostasis, inflammation, and cell survival. Human applications may include chronic liver diseases such as nonalcoholic steatohepatitis (NASH), acute organ injury such as Alcoholic Hepatitis (AH) and acute kidney injury (AKI), and inflammatory skin conditions such as psoriasis and atopic dermatitis. DURECT's advanced oral and injectable delivery technologies are designed to enable new indications and enhanced attributes for small-molecule and biologic drugs. Late stage product candidates in this category include POSIMIR® (bupivacaine extended release solution), an investigational locally-acting, non-opioid analgesic intended to provide up to 3 days of continuous pain relief after surgery, and ORADUR®-Methylphenidate ER Capsules, approved in Taiwan as Methydur Sustained Release Capsules, where it is indicated for the treatment of attention deficit hyperactivity disorder (ADHD). In addition, for the assignment of certain patent rights,DURECT receives single digit sales-based earn-out payments from U.S. net sales of Indivior's PERSERIS™ (risperidone) drug for schizophrenia, which was approved by the FDA in July 2018 and became commercially available in the U.S. in November 2018. For more information on DURECT, please visit www.www.durect.com.

DURECT Forward-Looking Statement

The statements in this press release regarding future events and expectations, including without limitationDURECT's plans to submit a full response to the FDA's Complete Response Letter, the time for the FDA to respond to such submission, the potential regulatory approval of POSIMIR by the FDA, the potential uses and benefits of POSIMIR and the possibility of finding a commercial partner for POSIMIR to provide financial resources that could be directed towards the development of DUR-928, as well as the potential benefits of DUR-928 to treat NASH and other hepatic and renal diseases, acute organ injury or inflammatory skin conditions such as psoriasis and atopic dermatitis, and the potential for DURECT to receive sales-based earn-out payments from Indivior from its sales of PERSERIS to treat schizophrenia are forward-looking statements involving risks and uncertainties that can cause actual results to differ materially from those in such forward-looking statements. Potential risks and uncertainties include, but are not limited to, the risks that the FDA will treat the Company's submission as a new NDA rather than a full response to the CRL, that the FDA will require additional trials or additional information regarding POSIMIR, the risk of potential adverse effects arising from the testing or use of DUR-928, the Company's ability to avoid infringing patents held by other parties and secure and defend patents of our own patents, and the Company's ability to manage and obtain capital to fund its operations and expenses. Further information regarding these and other risks is included in DURECT's Form 10-Q on November 8, 2018 under the heading "Risk Factors."

NOTE: ORADUR®, POSIMIR® and SABER® are trademarks of DURECT Corporation. Other referenced trademarks belong to their respective owners. DUR-928 and POSIMIR are drug candidates under development and have not been approved for

commercialization by the U.S. Food and Drug Administration or other health authorities. For PERSERIS full prescribing information, visit www.perseris.com.

View original content:http://www.prnewswire.com/news-releases/durect-announces-plans-to-submit-to-fda-a-full-response-to-the-posimir-complete-response-letter-300802689.html

SOURCE DURECT Corporation

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